CLAIM AMENDMENTS

1. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipients, wherein the composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and exhibits an $AUC/AUC_{Control}$ value of at least about 1.5, the AUC values being determined under similar conditions.

2. (currently amended) ~~A pharmaceutical~~ The composition according to claim 1, wherein the AUC/AUC_{Contol} value is at least about 1.75 or more such as, e.g., about 1.8 or more, about 1.9 or more, about 2.0 or more, about 2.5 or more, about 2.75 or more, about 3.0 or more, about 3.25 or more, about 3.5 or more, about 3.75 or more, about 4.0 or more, about 4.25 or more, about 4.5 or more, or about 4.75 or more, the AUC values being determined under similar conditions.

3. (currently amended) ~~A pharmaceutical~~The composition according to claim 1, wherein the AUC/AUC Control value is at least about 5.0 or more, about 6 or more, about 7 or more, about 8 or more, about 9 or more or about 10 or more, the AUC values being determined under similar conditions.

4. (currently amended) ~~A pharmaceutical~~ The composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipients, wherein the composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and exhibits a W_{50} that is about 2 hours or more such as, e.g., about 3 hours or more, about 4 hours or more, about 5 hours or more, about 6 hours or more, about 7 hours or more, about 8 hours or more, about 9 hours or more, about 10 hours or more, about 12 hours or more, about 14 hours or more, about 16 hours or more, about 18 hours or more or about 20 hours or more.

5. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient, wherein the

composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and exhibits a C_{diff} of 90 or less such as, e.g., about 85 or less, about 80 or less, about 75 or less, about 70 or less, about 65 or less, about 60 or less, about 55 or less ,about 50 or less, about 45 or less or about 40 or less, when C_{diff}= [C_{max} - C (t=7 hours)] and C_{diff} for Danocrine ® tablets is set to 100.

6. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient, wherein the composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and does not exhibit a significant adverse food effect as evidenced by a value of (AUC_{fed}/AUC_{fasted}) of at least about 0.85 with a lower 90% confidence limit of at least 0.75.

7. (currently amended) ~~A pharmaceutical~~ The composition according to claim 6, wherein the value of (AUC_{fed}/AUC_{fasted}) is about 0.9 or more such as, e.g., about 0.95 or more, about 0.97 or more or about 1 or more.

8. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together or an analogue thereof with one or more pharmaceutically acceptable excipient, wherein the composition upon oral administration to a mammal in need thereof releases danazol or an analogue thereof in a controlled manner and the composition being essentially bioequivalent with Danocrine ® or a similar commercially available danazol-containing product when administered in a dosis that is at the about most about 85% w/w of the dose of danazol administered in the form of Danocrine® or a similar commercially available danazol-containing product.

9. (currently amended) ~~A pharmaceutical~~The composition according to claim 8, wherein the dose is at the most about 80% w/w such as, e.g., at the most about 75%, at the most about 70% w/w, at the most about 65% w/w, at the most about 60% w/w, at the most about 55% w/w or at the most about 50% w/w of the dose of danazol administered in the form of Danocrine® or a similar commercially available danazol-containing product.

10. (currently amended) ~~A pharmaceutical~~The composition according to claim 8~~ or 9~~, wherein the bioequivalence is determined by means of at least one of the following parameters: t_{max}, c_{max}, AUC_{0-t}, $AUC_{0-infinity}$, W_{50}, W_{75} and/or MRT.

11. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient<u>s</u>, wherein the composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and reduces gastro-intestinal side effects compared to those of Danocrine® administered under the same conditions and in a dose that provides an equivalent therapeutic effect.

12. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient<u>s</u>, wherein the composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and reduces inter- and/or intra-individual variations compared to those of Danocrine® administered under the same conditions and in a dose that provides an equivalent therapeutic effect.

13. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient<u>s</u>, wherein the composition upon oral administration to a mammal in need thereof in a controlled manner releases at least about 50% w/w of the total amount of the active substance within about 15 hours such as, e.g., within about 12 hours.

14. (currently amended) A ~~pharmaceutical~~ composition according to claim 13, wherein the composition upon oral administration to a mammal in need thereof releases at least about 50% w/w of the total amount of the active substance within about 10 hours such as, e.g., within about 8 hours, within about 6 hours, within about 4 hours or within about 3 hours.

15. (currently amended) ~~A~~ <u>The</u> ~~pharmaceutical~~ composition according to claim 13~~ or 14~~, wherein the composition upon oral administration to a mammal in need thereof releases at least about

55% w/w such as, e.g., about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more or about 80% w/w or more of the total amount of the active substance within about 15 hours such as, e.g., within about 12 hours, within about 10 hours, within 8 hours or within about 6 hours.

16. (currently amended) ~~A pharmaceutical~~The composition according to claim 13, wherein at least about 50% w/w of the total amount of the active substance is released within 15 hours such as, e.g., within about 12 hours, when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

17. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of claims~~ claim 13-~~16~~, wherein at least about 50% w/w of the total amount of the active substance is released within about 10 hours such as, e.g., within about 8 hours, within about 6 hours, within about 4 hours, within about 3 hours or within about 2 hours, when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

18. (currently amended) ~~A pharmaceutical~~The composition according to claim 17, wherein at least about 50% w/w of the total amount of the active substance is released within about 1.5 hours such as, e.g., within about 1 hour, within about 0.75 hours, within about 0.5 hours or within about 20 minutes, when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

19. (currently amended) ~~A pharmaceutical~~ The composition according to ~~any of claims 13-18~~claim 13, wherein at least about 55% w/w such as, e.g., about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more or about 80% w/w or more of the total amount of the active substance thereof is released within about 15 hours such as, e.g., within about 12 hours, within about 10 hours, within 8 hours or within about 6 hours, when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

20. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of claims 13-18~~claim 13, wherein at least about 55% w/w such as, e.g., about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more or about 80% w/w or more of the total amount of the active substance is released within about 5 hours such as, e.g., within about 4 hours, within about 3 hours, within about 2 hours, within about 1 hours or within about 30 minutes, when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

21. (currently amended) ~~A~~ The pharmaceutical composition according to ~~any of claims 16-20~~claim 16, wherein the in vitro dissolution test is carried out employing USP dissolution test (paddle) and a buffer pH 7.5 containing 0.75% sodium lauryl sulfate as dissolution medium.

22. (currently amended) ~~A pharmaceutical~~The composition according to claim 13, wherein at least about 20% w/w such as, e.g., at least about 25% w/w, at least about 30% w/w, at least about 35% w/w or at least about 40% w/w of the total amount of the active substance is released within the first 3 hours such as, e.g., within the first 2 hours or within the first hour when tested in an in vitro dissolution test and employing a dissolution medium comprising a buffer having pH 7.5.

23. (currently amended) A ~~pharmaceutical~~ composition comprising danazol as an active substance together with one or more pharmaceutically acceptable excipient, wherein the composition upon oral administration to a mammal in need thereof has a delayed release of the active substance so that at the most about 10% w/w such as, e.g., at the most about 7.5% w/w or at the most about 5% w/w of the total amount of the active substance is released within the first two hours such as, e.g., within the first hour after administration.

24. (currently amended) ~~A pharmaceutical~~The composition according to claim 23, wherein at the most about 30% w/w such as, e.g., at the most about 25% w/w, at the most about 20% w/w, at the most about 15% w/w or at the most about 10% w/w of the active substance is released within 2 hours in an in vitro dissolution test employing a dissolution medium having a pH of at the most about 5 such as, e.g. at the most about 4.5, at the most about 4, at the most about 3.5, at the most about 3, at the most about 2 or at the most about 1.5.

25. (currently amended) ~~A pharmaceutical~~The composition according to claim 23~~ or 24~~, wherein at the most about 10% w/w such as, e.g., at the most about 7.5% w/w, at the most about 5% w/w or at the most about 2.5% w/w of the active substance is released within 2 hours in an in vitro dissolution test employing a dissolution medium having a pH of at the most about 5 such as, e.g. at the most about 4.5, at the most about 4, at the most about 3.5, at the most about 3, at the most about 2 or at the most about 1.5.

26. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of claims 23-25~~claim 23, wherein at the most about 60% w/w such as, e.g., at the most about 50% w/w, at the most about 40% w/w or at the most about 30% w/w of the active substance is released within 15 hours such as, e.g., within about 12 hours, when tested in an in vitro dissolution test employing a dissolution medium having a pH of at the most about 4.5 such as, e.g. at the most about 4.0, at the most about 3.5, at the most about 3, at the most about 2 or at the most about 1.5.

27. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of claims 23-26~~claim 23, wherein at the most about 40% w/w such as, e.g., at the most about 30% w/w, at the most about 25% w/w or at the most about 20% w/w of the active substance is released within 6 hours when tested in an in vitro dissolution test employing a dissolution medium having a pH of at the most about 4.5 such as, e.g. at the most about 4.0, at the most about 3.5, at the most about 3, at the most about 2 or at the most about 1.5.

28. (currently amended) ~~A pharmaceutical~~ The composition according to ~~any of claims 23-27~~claim 23, wherein at the most about 30% w/w such as, e.g., at the most about 25% w/w, at the most about 20% w/w or at the most about 15% w/w of the active substance is released within 4 hours when tested in an in vitro dissolution test employing a dissolution medium having a pH of at the most about 4.5 such as, e.g. at the most about 4.0, at the most about 3.5, at the most about 3, at the most about 2 or at the most about 1.5.

29. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding claims~~claim 1, wherein said composition is in the form of a particulate material that has a

geometric weight mean diameter d_{gw} of ≥ 10 µm such as, e.g. ≥ 20 µm, from about 20 to about 2000, from about 30 to about 2000, from about 50 to about 2000, from about 60 to about 2000, from about 75 to about 2000 such as, e.g. from about 100 to about 1500 µm, from about 100 to about 1000 µm or from about 100 to about 700 µm, or at the most about 400 µm or at the most 300 µm such as, e.g., from about 50 to about 400 µm such as, e.g., from about 50 to about 350 µm, from about 50 to about 300 µm, from about 50 to about 250 µm or from about 100 to about 300 µm.

30. (currently amended) ~~A~~ The ~~pharmaceutical~~ composition according to a~~ny of the preceding~~ ~~claims~~claim 1, wherein the one or more pharmaceutically acceptable excipients is selected from the group consisting of fillers, disintegrants, binders, diluents, lubricants and glidants.

31. (currently amended) ~~A pharmaceutical~~ The composition according to ~~any of the preceding~~ ~~claims~~claim 1 further comprising an pharmaceutically acceptable additive selected from the group consisting of flavoring agents, coloring agents, taste-masking agents, pH-adjusting agents, buffering agents, preservatives, stabilizing agents, anti-oxidants, wetting agents, humidity-adjusting agents, surface-active agents, suspending agents, absorption enhancing agents.

32. (currently amended) ~~A~~ The ~~pharmaceutical~~ composition according to ~~any of the preceding~~ ~~claims~~claim 1 wherein at least one of the one or more pharmaceutically acceptable excipients is selected from the group consisting of silica acid or a derivative or salt thereof including silicates, silicon dioxide and polymers thereof; magnesium aluminosilicate and/or magnesium aluminometasilicate, bentonite, kaolin, magnesium trisilicate, montmorillonite and/or saponite.

33. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding~~ ~~claims~~claim 32 ~~comprising~~ wherein the pharmaceutically acceptable excipient a silica acid or a derivative or salt thereof.

34. (currently amended) ~~A pharmaceutical~~The composition ~~any of the preceding claims~~ according to claim 32, wherein the pharmaceutically acceptable expient is ~~comprising~~ silicon dioxide or a polymer thereof.

35. (currently amended) ~~A pharmaceutical~~ The composition according to ~~any of the preceding~~claim ~~claims comprising a~~34, wherein the silicon dioxide product ~~that~~ has properties corresponding to Zeofree® 5161A, Zeofree® 5162, Zeofree® 5175A, Zeopharm® 80 (available from J. M. Huber, Hamina, Finland), Aeroperl® 300, Sident® 22S, Sipernat®160, Sipernat® 160PQ, Sipernat® 22, Sipernat® 22 LS, Sipernat® 22, Sipernat® 22 LS, Sipernat® 22S, Sipernat® 2200, Sipernat® 310, Sipernat® 320, Sipernat® 320 DS, Sipernat® 325 C, Sipernat® 35, Sipernat® 350, Sipernat® 360, Sipernat® 383 D8, Sipernat® 44, Sipernat® 44MS, Sipernat® 50, Sipernat® 50S, Sipernat® 50 S, Sipernat® 500 LS, or Sipernat® 570 ~~(available from Degussa. Frankfurt, Germany)~~.

36. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding claims~~claim 1, wherein said composition ~~comprising~~ comprises an oily material.

37. (currently amended) ~~A pharmaceutical~~The composition according to claim 36, wherein the concentration of the oily material in the composition is about 5% w/w or more such as, e.g., about 10% w/w or more, about 15% w/w or more, about 20% w/w or more, about 25% w/w or more, about 30% w/w or more, about 35% w/w or more, about 40% w/w or more, about 45% w/w or more, about 50 w/w or more, about 55% w/w or more, about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more, about 80% w/w or more, about 85% w/w or more, about 90% w/w or more or about 95% w/w or more.

38. (currently amended) ~~A pharmaceutical~~The composition according to claim 37, wherein the concentration of the oily material is in a range from about 20% to about 80% w/w such as, e.g., from about 25% to about 75% w/w.

39. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding claims~~claim 1, wherein at least a part of danazol is present in the form of a solid dispersion including a molecular dispersion and a solid solution.

40. (currently amended) ~~A pharmaceutical~~The composition according to claim 39, wherein the solid dispersion is manufactured by dissolving at least a part of danazol in an organic solvent containing a material suitable for forming solid dispersions and subsequent removing the organic solvent e.g. by evaporation.

41. (currently amended) ~~A pharmaceutical~~ The composition according to claim 40, wherein the material suitable for forming solid dispersions is selected from the group consisting of cellulose derivatives including hydroxypropylmethylcellulose, NaCMC, PVP and PVA.

42. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding claims~~claim 1 having an acceptable flowability as determined according to the method described in Ph.Eur. measuring the flow rate of the material out of a funnel with a nozzle diameter of 10.0 mm.

43. (currently amended) ~~A pharmaceutical G~~composition according to any of the preceding ~~claims for use in the manufacture of g~~granules, pellets, microspheres and~~,~~ nanoparticles comprising the composition of claim 1.

Claims ~~44~~-45 (canceled)

46. (currently amended) ~~A pharmaceutical~~The composition according to claim ~~44 or 45~~ in the form of tablets, capsules or sachets.

47. (currently amended) ~~A pharmaceutical~~The composition according to ~~any of the preceding claims for use in the manufacture of~~claim 46, wherein said tablets are obtained by direct compression.

48. (currently amended) A solid dosage form comprising ~~a pharmaceutical~~ the composition according to any of claim~~s 1-47~~ 1.

49. (currently amended) ~~A~~ The solid dosage form according to claim 48, wherein the concentration of the ~~pharmaceutical~~ composition in particulate form is in a range of from about 5% to 100% w/w such as, e.g., from about 10% to about 90% w/w, from about 15% to about 85% w/w, from about 20% to about 80% w/w, from about 25% to about 80% w/w, from about 30% to about 80% w/w, from about 35% to about 80% w/w, from about 40% to about 75% w/w, from about 45% to about 75% w/w or from about 50% to about 70% w/w of the dosage form.

50. (currently amended) ~~A~~ The solid dosage form according to claim 48, wherein the concentration of the ~~pharmaceutical~~ composition in particulate form is 50% w/w or more of the dosage form.

51. (currently amended) ~~A~~ The solid dosage form according to ~~any of claims 48-50~~claim 48, wherein the solid dosage form upon oral administration to a mammal in need thereof exhibits an $AUC/AUC_{Control}$ value of at least about 1.5, the AUC values being determined under similar conditions.

52. (currently amended) ~~A~~ The solid dosage form according to claim 51, wherein the $AUC/AUC_{Control}$ value is at least about 1.75 or more such as, e.g., about 1.8 or more, about 1.9 or more, about 2.0 or more, about 2.5 or more, about 2.75 or more, about 3.0 or more, about 3.25 or more, about 3.5 or more, about 3.75 or more, about 4.0 or more, about 4.25 or more, about 4.5 or more, about 4.75 or more, about 5.0 or more, about 6 or more, about 7 or more, about 8 or more, about 9 or more or about 10 or more, the AUC values being determined under similar conditions.

53. (currently amended) ~~A~~ The solid dosage form according to ~~any of claims 48-53~~claim 48, wherein the solid dosage form releases danazol in a controlled manner and does not exhibit a significant adverse food effect as evidenced by a value of (AUC_{fed}/AUC_{fasted}) of at least about 0.85 with a lower 90% confidence limit of at least 0.75.

54. (currently amended) ~~A~~ The solid dosage form according to claim 53, wherein the value of (AUC_{fed}/AUC_{fasted}) is about 0.9 or more such as, e.g., about 0.95 or more, about 0.97 or more or about 1 or more.

55. (currently amended) ~~A~~ The solid dosage form according to ~~any of claims 48-54~~claim 48, wherein the solid dosage form upon oral administration to a mammal in need thereof releases danazol in a controlled manner and the solid dosage form being essentially bioequivalent with Danocrine® or a similar commercially available danazol-containing product when administered in a dose that is at the most about 85% w/w of the dose of danazol administered in the form of Danocrine® or a similar commercially available danazol containing product.

56. (currently amended) ~~A~~ The solid dosage form according to claim 55, wherein the dose is at the most about 80% w/w such as, e.g., at the most about 75%, at the most about 70% w/w, at the most about 65% w/w, at the most about 60% w/w, at the most about 55% w/w or at the most about 50% w/w of the dose of the active substance administered in the form of Danocrine® or a similar commercially available danazol-containing product.

Claim 57 (canceled)